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Original Research

Investigations of factors affecting mortality in our ECMO (Extracorporeal membrane oxygenation) applications

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Abstract

Aim: Extracorporeal membrane oxygenation (ECMO) is a life support application used for life-threatening pulmonary or cardiac injuries that could not be treated with traditional treatment strategies successfully. In our study, we investigated factors affecting mortality in patients using ECMO in our clinic.

Material and Methods: In the study, 74 patients over the age of 18 who used ECMO were retrospectively examined. Patients were divided into two groups as those who survived after ECMO support (Group 1) and those who ended up with mortality (Group 2). Demographic data and comorbidities of patients, APACHE-2 score, RESP score, indications, applied ECMO type, inotropic treatments, blood products used and their quantities, non-ECMO support applications, and complications were studied.

Results: Of the 74 ECMO patients, 43 (58.11%) were male and 31 (41.89%) were female. The number of patients who ended up with mortality was 42(56.76%) and the number of those who survived was 32 (43.24%). Age, APACHE 2 and RESP scores, and ECMO flow were found to be statistically significantly higher in the group with mortality than the in the survival group ($p<0.05$). In addition, the rate of thrombocytopenia and the quantity of thrombocyte suspension used were higher in the mortality group. The causes of mortality were cardiac failure in 15 (35.71%) patients, hemorrhage in 7 (16.67%) patients, sepsis in 7 (16.67%) patients, multiple organ dysfunction in 6 (14.29%) patients, renal failure in 5 (11.9%) patients, and neurologic insufficiency in 2 (4.76%) patients.

Discussion: The mortality rate could be higher than the survival rate during ECMO applications as in our study. Knowing the causes of mortality is important to take measures.

Keywords

Extracorporeal Membrane Oxygenation (ECMO), Mortality, Survival

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Introduction

Extracorporeal membrane oxygenation (ECMO) is a life support application used for an acute and reversible pulmonary or cardiac injury that could not be successfully treated with traditional treatment strategies successfully, ECMO provides necessary oxygenation of the blood out of the body and has been increasingly used in intensive care units [1,2].

Extracorporeal life support was first used as salvage treatment in the mid-20th century in cardiac arrest patients who did not respond to traditional treatments. In the following period, oxygenators and centrifuge pumps of these support devices were miniaturized. The cardiac pulmonary machine has become compact and mobile and was implanted with thin-walled cannulas through peripheral routes. This has enabled ECMO application's widespread use [3].

ECMO devices used today are applied as venoarterial (VA) and venovenous (VV) according to the type of vein in which cannulation is performed. After oxygenation, blood from the venous system is given back to the body through the venous system with VV ECMO application. It is the VA ECMO application in which blood is taken from the venous system and given back to the body through the arterial system [2,4].

In our study, we aimed to investigate factors affecting mortality in patients using ECMO in our clinic.

Material and Methods

In this study, 74 patients over the age of 18 who underwent ECMO between 1 January 2010 and 1 January 2020 in Trabzon Ahi Evran Education and Research Hospital were evaluated retrospectively. Before the study, local ethic committee approval was taken according to the Helsinki declaration (2020/01). The inclusion criteria were patients over the age of 18 who underwent VA ECMO and VV ECMO applications. Exclusion criteria were patients under the age of 18 who underwent ECMO and those whose data could not have been obtained.

Patients were divided into two groups after ECMO support as those who survived (Group 1) and as those who ended up with mortality (Group 2). Demographic data of patients, comorbidities, APACHE-2 scores, RESP scores, ejection fraction values, indications of ECMO application, applied ECMO type (VV, VA), ECMO support durations, inotropic infusion treatments applied during ECMO support, non-ECMO support applications, complications of ECMO applications, blood products used and their quantities and early mortality rates (first 30 days) were examined and recorded. Data were reviewed retrospectively through patient files and patient information processing system.

Routine ECMO application procedure

Patients were monitored by invasive systemic arterial pressure monitoring with electrocardiography, SpO2 pulse oximetry, and radial artery cannulation preferably through a non-dominant arm. The right axillary region was opened in the patient who was scheduled for VA ECMO and arterial cannulation was performed with end-to-side anastomosis. Then, percutaneous venous cannulation was performed in the femoral vein and the patient was connected to ECMO. Distal circulation of the extremity was preserved in all patients by performing retrograde cannulation in the femoral artery. In addition, in the patient who was planned for VV ECMO, the first percutaneous venous catheter was inserted in the right jugular vein and then a percutaneous venous catheter in the femoral vein. Locations of cannulas were determined with a bedside ECHO. Time flow centrifugal pump (Jostra Rotaflow; Maquet Cardiopulmonary, Rastatt, Germany) and oxygenator (Jostra Quadrox; Maquet Cardiopulmonary, Rastatt, Germany) were used for the ECMO circuit. Before inserting cannulas into the patients, prime solution in the perfusion circuit was prepared with 1000 ml Ringer and unfractionated heparin (Koparin flakon, Koçak Farma, Turkey) was added initially.

Monitoring of the patients was performed daily, and upper and lower extremity pulses were evaluated for signs of hyper-perfusion and introduction site for signs of local bleeding and infection. All patients were monitored with a SpO2 monitor, invasive radial artery monitor, records of hemodynamic parameters, arterial blood gas monitor, daily physical examinations, and echocardiography (ECHO) investigations. Dexmedetomidine (Hipnodex flakon, Haver Farma, Turkey) infusion was started intravenously for sedation. After a bolus dose of 1 µg/kg was given intravenously to the patients, the maintenance infusion dose was administered as 0.2-0.7 µg/kg/hour. Anticoagulation was provided by unfractionated heparin (100 IU/kg), and monitored with activated coagulation time (ACT) measurements.

Criteria to separate from ECMO

Criteria to separate from ECMO were determined as stabilization of hemodynamic parameters, SvO2 level >70%, Htc between 28-30, normal lactate level, sufficient urinary output, and absence of bleeding or tamponade. Echocardiography examination before the separation showed that the left ventricular ejection fraction (EF) was >30%, and left ventricular distension and severe tricuspid insufficiency were absent. Decanulation in percutaneous ECMO applications was achieved by performing surgical repair of artery and vein used in femoral exploration under local anesthesia in extubated and under sedation in intubated patients.

Statistical Methods

Statistical analyzes of the collected data were performed with IBM SPSD 25 program. In the comparisons of survival and mortality groups, the Mann-Whitney U test was used to compare mean values and Fisher's exact test to compare frequencies. In the analysis, the significance limit was determined as 0.05.

Results

Of the 74 ECMO patients who were included in the study, 43 (58.11%) were male and 31 (41.89%) were female. VA ECMO was applied to 60 (81.08%) and VV ECMO to 14 (8.92%) patients. Indications for VA ECMO were the failure of cardiopulmonary bypass after cardiac surgery in 34 (56.67%) patients, cardiogenic shock in 14 (23.33%) patients, cardiac arrest after drug intoxication in 5 (8.33%) patients, bridge treatment in 4 patients who were scheduled for heart transplantation (6.67%), and peripartum cardiomyopathy in 3 (5%) patients. Indications for VV ECMO were pulmonary failure due to acute respiratory distress syndrome and pneumonia in 12 (85.71%) patients, and pulmonary emboli in 2 (14.29%) patients. Out of all cases, 32 (43.24%) survived and 42 (56.76%) ended up with mortality.

Demographic data of groups and comorbidities before the ECMO procedure are shown in Table 1.

Comparisons of data from groups during ECMO applications are shown in Table 2.

Causes of mortality were cardiac failure in 15 (35.71%) patients, hemorrhage in 7 (16.67%) patients, sepsis in 7 (16.67%) patients, multiple organ dysfunction (MODS) in 6 (14.29%) patients, renal failure in 5 (11.9%) patients, and neurologic insufficiency in 2 (4.76%) patients.

Table 1. Demographic data and comorbidities of the groups

Parameters	Group 1 (n=32)	Group 2 (n=42)	P*
Age (year) (mean ± SD)	50.47± 14.76	58.67 ± 14.38	0.019*
Male n (%)	18 (56.25)	25 (59.52)	0.795
Female n (%)	14 (43.75)	17 (40.48)	
Height (cm) (mean ± SD)	167.28±6.86	168.09±7.89	0.644
Weight (kg) (mean ± SD)	77.06±11.03	78.36±12.08	0.637
APACHE 2 (mean ± SD)	19.59±6.20	28.36±5.56	0.000*
RESP Score (mean ± SD)	2.44±3.17	-2.86±2.82	0.000*
Ejection Fraction (mean ± SD)	45.41±15.14	43.45±12.37	0.543
Hypertension n (%)	15 (46.87)	18 (42.86)	0.456
Coronary Artery Disease n (%)	17 (53.12)	24 (57.14)	0.456
Diabetes Mellitus n (%)	10 (31.25)	14 (33.33)	0.526
Renal Failure n (%)	9 (28.12)	11 (26.19)	0.529
COPD n (%)	5 (15.62)	7 (16.67)	0.582
Smoking n (%)	5 (15.62)	6 (14.29)	0.563

*P<0.05: Level of significance, SD: Standard deviation, n: Number, COPD: Chronic Obstructive Pulmonary Disease

Table 2. Comparisons of data of the groups during ECMO applications

Parameters	Group 1 (n=32)	Group 2 (n=42)	P*
ICU length of stay (day) (mean ± SD)	15.44±13.65	16.05±15.43	0.860
ECMO duration (day) (mean ± SD)	6.47±3.44	7.07±7.18	0.752
Inotrope-Vasopressor Use			
Dopamine n (%)	14 (43.75)	23 (54.76)	0.241
Dobutamine n (%)	18 (56.25)	29 (69.05)	0.187
Noradrenalin n (%)	15 (46.87)	30 (71.43)	0.028*
Adrenalin n (%))	-	8 (19.05)	-
IABP Use n (%)	11 (34.37)	15 (35.71)	0.551
ECMO Flow (ml/kg/min) (mean ± SD)	64.16±5.61	83.21±5.39	0.000*
ES (Unit) (mean ± SD)	6.41±4.48	7.86±8.23	0.371
FFP (Unit) (mean ± SD)	3.94±2.79	4.38±2.08	0.436
TS (Unit) (mean ± SD)	0.79±1.45	1.62±1.78	0.043*

P<0.05: Level of significance, SD: Standard deviation, n: Number, IABP: Intra-aortic Balloon Pump, ES: Erythrocyte Suspension, FFP: Free Frozen Plasma, TS: Thrombocyte Suspension.

Table 3. Comparisons of complications between groups

Parameters	Group 1 (n=32)	Group 2 (n=42)	P*
Bleeding n (%)	5 (15.62)	14 (33.33)	0.071
Thrombocytopenia n (%)	14 (43.75)	27(64.29)	0.064
Neurologic Complications n (%)	6 (18.75)	10 (23.81)	0.409
Renal Complications n (%)	5 (15.62)	7 (16.67)	0.582
Infection n (%)	11 (34.37)	20 (47.62)	0.183
Metabolic Complications n (%)	3 (9.37)	6 (14.29)	0.395
Vascular Complications n (%)	1(3.12)	3 (7.14)	0.417

P<0.05: Level of significance, SD: Standard deviation, n: Number

Discussion

ECMO is one of the most important treatment methods for resistant pulmonary and cardiac failure today. The operating principle of ECMO is to take blood with a cannula applied to a large vessel through percutaneous and surgical ways, oxygenate it on the artificial membrane, and give it back to the patient [5,6].

In adult patients, ECMO treatment is performed as VA and VV ECMO. Their indications are different. The indications of VA ECMO are cardiogenic shock (acute myocardial infarction, myocarditis), inability to separate from cardiopulmonary bypass after cardiac surgery despite conventional treatments (fluid resuscitation, vasopressor, inotropic), deep cardiac arrest due to drug intoxication, cardiogenic shock secondary to right ventricular failure after pulmonary embolism, bridge treatment in patients awaiting heart transplantation, graft failure after heart transplantation and cardiogenic shock secondary to acute allograft rejection [6,7]. The indications for VV ECMO are end-stage pulmonary disease secondary to chronic obstructive pulmonary disease, acute respiratory distress syndrome, bronchiectasis and cystic fibrosis, pneumonia, graft failure after lung transplantations, pulmonary hypertension, pulmonary embolism, smoke inhalation, meconium aspiration and respiratory arrest [7,8]. In our study, the indications of VA ECMO were inability to separate from cardiopulmonary bypass after cardiac surgery, cardiogenic shock, cardiac arrest due to drug intoxication, bridge treatment in patients awaiting heart transplantation, peripartum cardiomyopathy, while the indications of VV ECMO were pulmonary failure due to acute respiratory distress syndrome, pneumonia and pulmonary embolism. These are in parallel to the literature.

Like all interventional procedures, in patients undergoing ECMO, it is important to determine mortality rates and factors affecting mortality. In our study, the 30-day mortality rate was 56.76%. In studies in the literature, the reported mortality rate (55-84%) was similar to our study [9-13].

In studies, the age of the patient was determined as an important factor for mortality, and as the mean age increased, mortality also increased. In addition, it has been reported that when these surviving patients are admitted to intensive care units, the APACHE 2 scores are lower [14,15]. In our study, we determined that age and APACHE 2 score affect mortality, and as these two figures decreased, mortality rate also decreased (Table 1).

Comorbidities accompanying ECMO applications also affect mortality. While coronary artery disease, diabetes mellitus, renal failure, and obesity are reported to be related to mortality, hypertension, and chronic obstructive pulmonary disease are also risk factors [9,10,16]. In both groups, the most common comorbidities were coronary artery disease, hypertension, and diabetes mellitus. There was no statistically significant difference when the two groups were compared in terms of comorbidities (Table 1).

RESP score which was developed to predict survival during ECMO was determined to be statistically significantly higher in

the mortality group (Table 1). In the study by M. Schmidt et al, a similar result was obtained [17].

In our study, rates of ICU admission and ECMO duration were found to be lower in the survival group when compared to the mortality group (Table 2). Of course, these durations vary from patient to patient. The important thing is to allow the patient to spend enough time connected to the ECMO device to let the lung and heart recover adequately. In the patient group whose management is very difficult and complicated, early separation from the ECMO device might cause unfavorable outcomes.

ECMO application is a valuable treatment modality in patients who develop low cardiac output syndrome after cardiac surgery, and who have heart failure with very low ejection fraction values in intensive care units. With the help of ECMO, myocardial injury is a result of high dose inotropic agent use by providing circulation support early. In the literature, it has been reported that increased contractility and temporary improvement in cardiac performance due to the use of inotropic agents might lead to increased myocardial energy consumption, perfusion - contraction mismatch with increased anaerobic glycolysis, myocardial necrosis, and, as a result, the risk of progression to heart failure [18]. Thus, it is possible to associate the use of high dose inotropic before and after ECMO with heart failure and increased mortality. In our study, there was a lower need for inotropic agents in surviving patients, and noradrenalin use in the mortality group was statistically significantly higher (Table 2).

There are conflicting results in the literature on the usefulness of simultaneous intra-aortic balloon pump (IABP) use with ECMO. Brechot N et al noted in their study that there was a significant decrease in radiographic findings of pulmonary edema and shorter use of mechanical ventilation compared to VA ECMO alone, and concluded that combined IABP-ECMO use had some favorable results [19]. In a retrospective study with a large patient population size in the literature, it was reported that IABP does not affect survival [20]. In our study, simultaneous use of IABP was examined but there was no significant difference between groups in terms of IABP use (Table 2).

ECMO flow is reported as another important parameter affecting mortality in the literature. According to the results of a study, it was reported that the high flow of ECMO especially in the first 24th hour is associated with mortality [21]. In our study, when the patients were evaluated in terms of ECMO flow, ECMO flow in the 24th hour was statistically significantly faster in the mortality group (Table 2).

In ECMO applications, hemorrhage is a common complication. In particular, bleeding is one of the leading causes of mortality [22,23]. In addition, it was reported that the use of blood products is associated with mortality [9]. In our study, the use of blood products and thrombocyte suspension was found to be statistically significantly higher in the mortality group (Table 2). Another hematologic complication of ECMO that increases use of blood products and bleeding is thrombocytopenia. It was reported in the literature that thrombocytopenia could be detected in patients already admitted to intensive care units and is associated with the risk of bleeding and mortality [24]. In our study, thrombocytopenia and associated bleeding rate were higher in the mortality group (Table 3).

MODS and myocardial failure are also other important causes of mortality. In the study by Rastan AJ et al, the most common cause of mortality was reported as acute myocardial failure [9]. In another study, it was MODS [13]. In our study, cardiac failure, hemorrhage, sepsis, and MODS were found to be causes of mortality.

The limitations of our study were that the number of patients was small and it was retrospective in nature.

Conclusion

ECMO application is an important supportive treatment method for pulmonary and cardiac failure. During this application, mortality could reach higher rates than survival, as in our study. Predicting the causes of mortality and knowing the risks of encountering these is important to take necessary measures. Further prospective studies with more patients are needed in this field.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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